Referrals in Acute Coronary Events for CARdiac Catheterization: The RACE CAR trial

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BACKGROUND: Women with acute coronary syndromes have lower rates of cardiac catheterization (CC) than men.
OBJECTIVE: To determine whether sex/gender, age, risk level and patient preference influence physician decision making to refer patients for CC.
METHODS: Twelve clinical scenarios controlling for sex/gender, age (55 or 75 years of age), Thrombolysis in Myocardial Infarction risk score (low, moderate or high) and patient preference for CC (agreeable or refused/no preference expressed) were designed. Scenarios were administered to specialists across Canada using a web-based computerized survey instrument. Questions were standardized using a five-point Likert scale ranging from 1 (very unlikely to benefit from CC) to 5 (very likely to benefit from CC). Outcomes were assessed using a two-tailed mixed linear regression model.
RESULTS: Of 237 scenarios, physicians rated men as more likely to benefit from CC than women (mean [± SE] 4.44±0.07 versus 4.25±0.07, P=0.03), adjusted for age, risk and patient preference. Low-risk men were perceived to benefit more than low-risk women (4.20±0.13 versus 3.54±0.14, P<0.01), and low-risk younger patients were perceived to benefit more than low-risk older patients (4.52±0.17 versus 3.22±0.16, P<0.01). Regardless of risk, patients who agreed to CC were perceived as more likely to benefit from CC than patients who were disagreeable or made no comment at all (5.0±0.23, 3.67±0.21, 2.95±0.14, respectively, P<0.01).
CONCLUSION: Canadian specialists' decisions to refer patients for CC appear to be influenced by sex/gender, age and patient preference in clinical scenarios in which cardiac risk is held constant. Future investigation of possible age and sex/gender biases as proxies for risk is warranted.

Key Words: *Acute coronary syndromes; Cardiac catheterization; Gender; Decision making*

L'essai RACE CAR sur les aiguillages de cathétérisme cardiaque en cas d'événements coronariens aigus

HISTORIQUE : Les femmes ayant un syndrome coronarien aigu présentent un taux de cathétérisme cardiaque (CC) plus faible que les hommes.
OBJECTIF : Déterminer si le sexe, l'âge, le niveau de risque et la préférence du patient influent sur la décision du médecin à aiguiller les patients vers un CC.
MÉTHODOLOGIE : Les chercheurs ont conçu 12 scénarios cliniques tenant compte du sexe, de l'âge (de 55 à 75 ans), de l'indice de risque de thrombolyse en cas d'infarctus du myocarde (faible, modéré ou élevé) et de la préférence du patient à subir un CC (en accord, refus ou aucune préférence exprimée). Ils ont administré les scénarios à des spécialistes du Canada au moyen d'un sondage informatisé rempli par Internet. Ils ont normalisé les questions au moyen d'une échelle Likert de cinq points variant de 1 (très peu susceptible de profiter du CC) à 5 (très susceptible de profiter du CC). Ils ont évalué les résultats au moyen d'un modèle de régression linéaire bilatéral mixte.
RÉSULTATS : Dans les 237 scénarios, les médecins ont classé les hommes comme plus susceptibles que les femmes de profiter du CC (moyenne±ÉT 4,44±0,07 par rapport à 4,25±0,07, P=0,03), après rajustement selon l'âge, le risque et la préférence du patient. Les hommes à faible risque étaient perçus comme en profitant davantage que les femmes à faible risque (4,20±0,13 par rapport à 3,54±0,14, P<0,01), et les patients plus jeunes à faible risque, davantage que les patients plus âgés à faible risque (4,52±0,17 par rapport à 3,22±0,16, P<0,01). Quel que soit le risque, les patients qui acceptaient de subir le CC étaient perçus comme plus susceptibles d'en profiter que ceux qui y étaient réfractaires ou qui n'exprimaient pas de préférence (5,0±0,23, 3,67±0,21, 2,95±0,14, respectivement, P<0,01).
CONCLUSION : La décision des spécialistes canadiens d'aiguiller les patients vers un CC semble être influencée par le sexe, l'âge et la préférence des patients dans les scénarios clinique où le risque cardiaque est maintenu constant. De futures explorations sur les biais éventuels relativement à l'âge et au sexe comme indications du risque s'imposent.

It has been widely reported that coronary artery disease (CAD) is the leading cause of morbidity and mortality of both men and women in westernized countries, accounting for over one-third of total deaths (1). Furthermore, CAD accounts for the greatest proportion of deaths among women of all ages, yet despite this, it has often been viewed as a 'man's disease'. Although there are similarities, differences do exist, particularly in symptom presentation and risk profile, because women characteristically present with CAD at older ages than men (2-23), and more often with atypical symptoms (2,8,10,13,17,18). However, women generally have less severe CAD as determined by angiography (4,8,10-12,16,22,23,24-28), contributing to the perception that they are at lower risk. Differences in physicians' interpretations of symptoms, risk assessment and patient preferences may contribute to sex differences in the diagnosis and treatment of CAD (29). Women generally receive less medical therapy, and are referred less frequently for angiography, percutaneous coronary interventions and bypass graft surgery than men (4,10-12,16,23,30). Even among women with acute coronary syndrome (ACS), studies have reported that women are referred less often for invasive procedures than men (16,31,32). The implications of these findings have been controversial, suggesting higher mortality and poorer long-term survival among women (2,10,16,21,31,32). Interestingly, a growing body of literature cautions that age may be an important confounder in the sex/gender literature. Studies (21,22) have found that among patients postmyocardial infarction (MI) and postbypass graft surgery, mortality was up to three times higher among younger women compared with their young male counterparts, even after adjusting for

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possible comorbidities. The higher risk of mortality in these young women may be due, in part, to the perception that women, especially younger women, are at very low risk for CAD. At the same time, previous studies (33) consisting mostly of retrospective analyses of administrative databases or subgroup analyses of clinical trials, have generally suffered from methodological limitations including the lack of statistical power to determine whether true differences exist.

The proposed study is an effort to prospectively assess whether sex/gender independently influences physician decision making among various profiles of patients with ACS, with the following primary objectives: to determine whether there is a difference among Canadian cardiologists' and internal medicine specialists' decisions to refer male and female patients of equal risk for cardiac catheterization (CC); and to determine patient factors that influence referral decisions including age, sex/gender, risk level and expressed preference for catheterization. Secondary objectives include the following: to determine factors that influence the perceived risk a patient will suffer from an MI within the next 14 days; the characterization of chest pain; the probability a patient has significant CAD; and patient opinion in physician decision making for referral for CC.

METHODS

For the purpose of the present paper, the term 'sex' refers to the biological and physiological determinants of disease, and 'gender' refers to a person's social roles as expressed through their values and beliefs, psychosocial characteristics and behaviours (24).

Design of survey instrument

Twelve clinical vignette scenarios describing patients presenting to the emergency room with chest pain were designed, controlling for all combinations of patient factors, including two age categories (55 or 75 years of age), three Thrombolysis in Myocardial Infarction (TIMI) risk levels (low, moderate and high) and two patient preferences (patient expressed preference and no preference expressed) for catheterization. Due to sample size concerns, the scenarios were designed with blank fields in place of 'gender', and a computer program was designed to randomly allocate sex/gender and sex/gender-specific pronouns to each scenario. In addition, gender-specific terms were matched and tagged to the randomly assigned sex, to deliberately tap into physician perceptions that may be associated with gender. Each physician was required to review and assess three randomly allocated vignette scenarios: one each of male, female and sex/gender neutral. After reading each clinical vignette scenario, physicians were required to answer a series of standardized questions about the patient. Physicians were blinded to the primary objective of the study. Physicians also provided demographic information about their practices. The scenarios were pretested for face validity using the American College of Cardiology/American Heart Association criteria for referral for catheterization (34). Before initiation of the study, pilot testing was administered, appropriately modifying the scenarios and computer program to work out any issues such as the design of 'limits' to ensure that there were no missing data fields. The design of the present study was inspired by and modelled after a study by Schulman et al (29). An example of a clinical vignette scenario is provided in Appendix A.

Survey administration

To recruit physicians for the present study, an e-mail with a link to the study's website was sent to cardiologists and internal medicine specialists from across Canada using the following sources: Canadian Cardiovascular Society (CCS) list of internal medicine and cardiology specialist regular members; a Canada-wide list of cardiologists in the Canadian Medical Association (CMA) directory (excluding previous CCS respondents); and colleagues and collaborators from across Canada, in addition to referring physicians at McMaster University (Hamilton, Ontario) who were not represented by the CCS or the CMA list.

Up to three e-mails describing the study, with a link to the website, were sent, each two weeks apart. Follow-up telephone calls were made to physicians on the CMA list, and the collaborators and colleagues list, which were subsequently followed with personally addressed e-mails as friendly reminders. There was no financial compensation for participation in the study; however, as an incentive, a draw for a gift certificate to a bookstore was proposed.

Controlled patient factors

The scenarios contained patient factors representing all possible combinations of variables of interest. The scenarios were controlled for sex/gender of the patient (male, female or sex/gender neutral), age (55 versus 75 years of age), level of TIMI risk score (low, moderate or high) and the patient's preference for CC (no preference expressed or preference expressed [which was further subdivided into agreeable toward or refused CC]).

Description of physician and hospital characteristics

Physician information was collected to understand and contextualize the sample population's demography and practice patterns including physician sex, type of specialty (internal medicine, cardiology or subspecialities within cardiology), years since graduation from medical school, an estimate of the percentage of female patients seen in practice, an estimate of the percentage of white Caucasian patients seen in practice, and if the physician used any type of risk assessment score in deciding whether to refer a patient for catheterization. Hospital factors included geographical region, the presence or absence of on-site catheterization facilities and type of practice (academic centre, community-based, outpatient clinic only or other). The full list of physician demographics and hospital characteristics is available in Appendix B.

Survey questions

Physicians were blinded to the primary objective of the study, namely to detect a sex/gender bias for CC. Physicians were asked to assess the likelihood that a patient would benefit from CC on a five-point Likert scale ranging from 1 (very unlikely to benefit from CC) to 5 (very likely to benefit from CC). Physicians were also asked to characterize the patient's chest pain (noncardiac, possibly cardiac or definitely cardiac), the risk level of suffering a fatal or nonfatal MI in the next 14 days (low risk, moderate risk or high risk) and the probability that the patient has significant CAD (defined as a stenosis of 70% or greater of at least one major epicardial vessel) on a five-point Likert scale ranging from 1 (very unlikely) to 5 (very likely). Physicians who decided not to refer the patient for CC were asked if they would order any further tests and, if so, which tests. Physicians were also asked to report how much patient opinion influences their decision to refer a patient for CC, ranging from 1 (not much at all) to 5 (to a great extent). Finally, physicians were requested to report if they required any other information to make their decision for catheterization referral. The full list of vignette questions and scaling is available in Appendix C.

Statistical considerations

Statistical power: It was predetermined that 68 physicians completing three scenarios each, for a total of 204 scenario assessments, would be required to provide 90% power to detect a minimum difference of 10% in CC rate between men and women. The sample size calculation included the clustering effect of physicians, assuming an intracluster correlation coefficient of 0.5.

Analysis: To assess the differences in physician decision making to refer a patient for CC, a mixed linear model was used. Patient factors were represented as covariates and analyzed as fixed effects, which included the controlled patient factors of sex/gender, age, TIMI risk level and the patient's preference for catheterization. Interactions of all combinations of patient factors were also tested in the mixed effects model. Design variables were created for categorical variables. Because each physician answered standardized questions for three scenarios, scores for each physician rater were clustered and analyzed as a random effect. Sidak's correction was used to adjust for multiple testing. Significance testing was evaluated using two-tailed testing, with data presented as mean ± SE. All analyses were performed using SPSS 16.0 statistical software (SPSS Inc, USA).

TABLE 1
Participating physician demographics and hospital factors

Characteristics	Physicians (n=79), n (%)
Physicians	
Male physician	69 (87.3)
Speciality	
Cardiology	72 (91.1)
Internal medicine	7 (8.9)
Years practicing	
<10	21 (26.6)
10 to <20	31 (39.2)
20 to <30	22 (27.8)
≥30	5 (6.3)
Female patients seen in practice (n=76), %	
<35	10 (13.2)
35 to <50	45 (59.2)
≥50	21 (27.6)
Nonwhite patients seen in practice (n=72), %	
<10	14 (19.4)
10 to <25	33 (45.8)
25 to <40	16 (22.2)
≥40	9 (12.5)
Risk score used (n=72)	
No	37 (51.4)
Yes	35 (48.6)
TIMI risk score	26 (74.3)
Hospitals	
Presence of catheterization facilities	49 (62.0)
Academic centre	58 (73.4)
Region of Canada	
West	18 (22.8)
Ontario or Quebec	56 (70.9)
Atlantic	5 (6.3)

TIMI Thrombolysis in Myocardial Infarction

TABLE 2
Benefit from cardiac catheterization controlled for sex/gender, age, Thrombolysis in Myocardial Infarction risk score and patient preference about cardiac catheterization (CC)

Variable	Benefit likelihood, mean ± SE	P
Sex/gender		
Male	4.44±0.07	0.03
Female	4.25±0.07	
Age, years		
55	4.55±0.09	0.01
75	4.14±0.09	
Level of risk		
Low	3.87±0.1	<0.01
Moderate	4.25±0.1	
High	4.93±0.08	
Expressed preference		
Agreeable for CC	4.65±0.13	0.01
Disagreeable for CC	4.17±0.12	
No opinion	4.21±0.08	

What is the likelihood this patient would benefit from a CC procedure? Score: 1 = very unlikely to 5 = very likely

RESULTS

Baseline demographics of physicians and their institutions

After sampling almost 700 physician specialists across Canada at multiple time intervals, a total of 79 physicians (11%) each completed three randomly assigned scenarios, for a total of 237 scenarios, between July and August 2006.

Physician characteristics

The baseline demographic information of the participating physicians is outlined in Table 1. Briefly, physicians participating in the present study were mostly men (87%) and specialized in cardiology (91%). The sample of physicians were experienced, with the majority of participating physicians practising for over 10 years; only one-quarter of physicians reported having less than 10 years of cardiology work experience. The percentage of female patients seen in practice varied, with 72% of physicians reporting that female patients comprised 50% or less of their practice, and only one-quarter of physicians reported that women comprised more than 50% of their practice. Similarly, the ethnic makeup of cardiology practices across Canada revealed that nonwhite patients comprise less than 25% of physician practices in the majority of practices. In addition, when physicians were asked if they used a risk score when assessing their patients, approximately one-half reported that they used a risk score. Of the number of physicians who used a risk score, 74% reported the TIMI risk score as their risk assessment score of choice (Table 1).

Hospital factors

Geographically, 70% of physicians practised in Ontario or Quebec, 23% practised in the western provinces and 6% of participating physicians practised in Atlantic Canada. Also, two-thirds of physicians reported the presence of catheterization laboratories at their institutions, and 73% worked at academic centres (Table 1).

Referral decisions based on sex/gender, age, patient preference and risk

Physicians rated men as more likely to benefit from CC than women (mean [± SE] score = 4.44±0.07 versus 4.25±0.07, P=0.03), controlling for age, risk level and expressed preference for a catheterization procedure (Table 2). Younger patients (55 years of age) were rated as more likely to benefit from catheterization than older patients (75 years of age) controlled for all patient factors (4.55±0.09 versus 4.14±0.09, P=0.01). Benefit from catheterization increased as the level of risk increased (low TIMI risk = 3.87±0.1, moderate TIMI risk = 4.25±0.1, high TIMI risk = 4.93±0.08, P<0.01). Patients who agreed to undergo CC were rated as more likely to benefit from the procedure than patients who would not or expressed no opinion, even after controlling for sex/gender, age and risk ('agreeable' = 4.65±0.13 versus 'refused' = 4.17±0.12 versus 'no opinion = 4.21±0.08, P=0.01) (Table 2).

Interactions between patient factors influencing referral decisions

Physicians rated low TIMI risk men as more likely to benefit from CC than low TIMI risk women (4.20±0.13 versus 3.54±0.14, respectively, P<0.01), controlling for all other patient factors. No significant differences were detected among moderate and high TIMI risk men and women (Table 3).

Physicians rated younger, low TIMI risk patients as more likely to benefit from CC than older, low-risk patients (4.52±0.17 compared with 3.22±0.16, respectively, P<0.01). No significant differences were detected between moderate-risk and high-risk, or 55-year-old and 75-year-old patients (Table 3).

When analyzing physician perceptions of CC benefit according to risk, patient preference influenced physician decision making. Low TIMI risk patients who agreed to undergo CC were perceived as more likely to benefit than low TIMI risk patients who would not undergo the procedure or made no comment at all (all low-risk patients: 'agreeable' = 5.0±0.23 compared with 'refused' = 3.67±0.21 and 'no opinion' = 2.95±0.14, P<0.01). No significant differences were detected among high-risk patients, regardless of the patient's expressed preference for the procedure, because physicians rated all high-risk patients to significantly benefit from CC (Table 3).

When considering physician perception of benefit from CC according to patient preference, TIMI risk level did not seem to influence physician decision making. Among patients who agreed to CC, low-risk patients were shown to benefit more than moderate-risk patients and equally as much as high-risk patients (all patients agreeable for CC: low risk = 5.0±0.23 versus moderate risk = 4.06±0.24 and high-risk = 4.88±0.17, P<0.01). Among patients who did not want CC or who did not express an opinion about the procedure, the benefit of catheterization reflected the main effects observed, where benefit from catheterization increased according to increasing risk (Table 3).

TABLE 3
Interaction of patient benefit from cardiac catheterization (CC) referral between Thrombolysis in Myocardial Infarction (TIMI) risk score, and gender, age and patient preference

	Benefit likelihood, mean ± SE		
	Low TIMI risk	Moderate TIMI risk	High TIMI risk
Sex/gender			
Male	4.20±0.13*	4.16±0.12	4.97±0.11
Female	3.54±0.14*	4.33±0.13	4.88±0.11
Age, years			
55	4.52±0.17*	4.13±0.15	4.98±0.13
75	3.22±0.16*	4.36±0.17	4.85±0.14
Patient preference			
Agreeable for CC	5.00±0.23*	4.06±0.24*	4.88±0.17*
Disagreeable for CC	3.67±0.21*	3.93±0.2*	4.92±0.2*
No opinion	2.95±0.14*	4.74±0.13*	4.94±0.12*

*What is the likelihood this patient would benefit from a CC procedure? Score: 1 = very unlikely to 5 = very likely. *P<0.01*

Secondary objectives

Risk of suffering an MI within the next 14 days: As an internal measure of validity of the TIMI risk score used to determine controlled risk in the present study's scenarios, physicians were asked to rate the level of risk (according to the TIMI risk criteria) that the described patient would suffer a fatal or nonfatal MI in the next 14 days. It was found that physicians in the present study appropriately identified low-, moderate- and high-risk patients according to TIMI risk criteria (P<0.01) (Table 4). There were no statistically significant differences detected in the risk of suffering an MI according to sex/gender, age or patient preference. However, an interaction was detected between age and sex/gender; physicians rated 55-year-old men as more likely to be at risk for an MI than 55-year-old women controlled for all other patient factors (2.62±0.09 versus 2.32±0.09, respectively, P<0.01 [interaction not presented in table]).

Characterization of chest pain: Physicians were asked to characterize patient chest pain on a three-point Likert scale (1 = noncardiac, to 3 = definitely cardiac). Physicians rated chest pain among men as more likely to be cardiac compared with the same pain among women, even when data analysis was controlled for all other patient factors (men = 2.66±0.04 versus women = 2.53±0.04, P=0.02). Patients were rated as more likely to be experiencing cardiac pain if they were younger (55 years of age = 2.77±0.05 versus 75 years of age = 2.43±0.05, P<0.01) or had higher TIMI risk (low TIMI risk = 2.36±0.05, moderate TIMI risk = 2.48±0.05 and high TIMI risk = 2.95±0.05, P<0.01). Physicians were more likely to characterize chest pain in an older low-risk patient as more cardiac in nature than in a young low-risk patient, even after controlling for all other patient factors (1.93±0.07 versus 2.79±0.09, respectively, P<0.01 [interaction not presented in table]). No differences were found between younger and older patients of moderate or high-risk. Physicians were not influenced by the patient's preference for CC (P=0.10) (Table 4).

Estimated probability that patient has significant obstructive CAD: When physicians were asked to estimate the probability that the described patient has significant CAD on a five-point Likert scale (1 = very unlikely, to 5 = very likely), physicians rated men as more likely to have significant CAD than women, controlling for all other patient factors (men = 4.67±0.07 versus women = 4.38±0.07, P=0.01). Also, the probability that the patient may have significant CAD increased as the level of TIMI risk increased (low TIMI risk = 4.25±0.09, moderate TIMI risk = 4.43±0.09 and high TIMI risk = 4.89±0.08, P<0.01). Differences in the probability of the patient having significant CAD were not detected among patients of different ages (Table 4).

Among women who did not want a CC procedure, physicians were less likely to suspect significant CAD, compared with women who were agreeable or who had no opinion about the procedure ('refused' = 3.85±0.14 versus 'agreeable' = 4.62±0.13 and 'no opinion' = 4.66±0.1, P<0.01).

TABLE 4
Influence of secondary objectives controlled for sex/gender, age, Thrombolysis in Myocardial Infarction (TIMI) risk score and patient preference

	Estimated risk of myocardial infarction*		Chest pain characterization†		Probability of significant CAD‡		Influence of patient opinion§	
Controlled patient variable	Mean ± SE	P	Mean ± SE	P	Mean ± SE	P	Mean ± SE	P
Sex/gender		0.12		0.02		0.01		0.39
Male	2.47±0.06		2.66±0.04		4.67±0.07		2.90±0.14	
Female	2.34±0.06		2.53±0.04		4.38±0.07		2.99±0.14	
Age, years		0.26		<0.01		0.53		0.43
55	2.47±0.07		2.77±0.05		4.57±0.08		3.03±0.16	
75	2.34±0.08		2.43±0.05		4.48±0.09		2.87±0.17	
TIMI risk		<0.01		<0.01		<0.01		<0.01
Low	1.95±0.08		2.36±0.05		4.25±0.09		3.23±0.17	
Moderate	2.36±0.08		2.48±0.05		4.43±0.09		2.97±0.17	
High	2.90±0.06		2.95±0.05		4.89±0.08		2.64±0.15	
Patient preference		0.43		0.10		<0.01		0.28
Agreeable for CC	2.47±0.08		2.58±0.07		4.71±0.09		2.69±0.21	
Disagreeable for CC	2.39±0.09		2.69±0.07		4.29±0.1		3.12±0.21	
No opinion	2.35±0.06		2.53±0.04		4.57±0.07		3.03±0.15	

**How would you characterize this patient's level of risk of suffering a fatal or nonfatal myocardial infarction in the next 14 days? Score: 1 = low risk, 2 = moderate risk, 3 = high risk; †How would you characterize this patient's chest pain? Score: 1 = noncardiac, 2 = possibly cardiac, 3 = definitely cardiac; ‡Estimate the probability that this patient has significant coronary artery disease (CAD) (stenosis greater than 70%). Score: 1 = very unlikely to 5 = very likely; §How much does the patient's opinion influence your decision to refer them for cardiac catheterization (CC)? Score: 1 = not very much to 5 = very much*

Influence of patient opinion for referral for CC: Physicians were asked to rate the degree to which a patient's opinion influences their decision to refer a patient for CC on a five-point Likert scale (1 = not very much, to 5 = very much). Physicians reported that they are not swayed by the patient's opinion according to sex/gender, age or their expressed preference for a CC procedure; rather, the level of TIMI risk was a statistically significant influential factor when a physician considered the patient's opinion in deciding to refer a patient for catheterization (low TIMI risk = 3.23±0.17, moderate TIMI risk = 2.97±0.17, high TIMI risk = 2.64±0.15, P<0.01) (Table 4).

DISCUSSION

Our study indicates that among Canadian specialists, women are perceived to benefit less from CC than men of equal age, risk and expressed preference for catheterization. In addition, specialists perceive younger patients as more likely to benefit from CC than older patients, high-risk patients to benefit more than low-risk patients, and patients agreeable for CC as more likely to benefit than patients who refuse or express no opinion at all.

The results from our study support those in the literature that indicate women are less often referred for cardiac procedures than men (4,10-12,23,29,30,35,36). Although post hoc hypotheses have alluded to sex/gender differences in the past, our study is unique in that physician decision making was prospectively assessed, unlike previous studies that depended on retrospective data collection, database analysis or post hoc analyses of larger trials with insufficient power to detect sex/gender differences. The sex/gender difference in catheterization benefit that we detected was consistent across all models, which were controlled for age, risk and patient preference. We were able to explain some of the sex/gender difference due to risk. The interaction between TIMI risk and sex/gender suggests that among patients who were truly at low risk, women were evaluated appropriately as such, whereas low-risk men were perceived to gain more benefit from CC. Previously published literature (16,35) has suggested that, perhaps, women are being appropriately treated, and men undergo an excessive number of CCs, and our results lend support to this. It is possible that symptoms and risk factors in men may be over estimated, while symptoms and risk factors in women may be appropriately estimated. Our results support this because cardiac chest pain and significant stenotic disease were perceived to be more likely among men than women across scenarios controlled for sex/gender, age, TIMI risk and patient preference. Although this perspective may seem somewhat confusing, it is not contradictory. CC is the gold standard in CAD diagnosis. Evidence shows that high-risk patients have the most to gain from CC; by identifying these patients, treatment options to improve prognosis can be offered including surgical revascularization. However, beyond risk factor modification, much debate surrounds treatment options for low- and moderate-risk patients, implying that 'benefit' from CC is unknown. Currently, we do not know what the 'catheterization-benefit' threshold is for lower risk patients. We have demonstrated that there is a perception by physicians that women are at 'lower risk' for CAD and, therefore, will not 'benefit' from CC. We are not suggesting that this perception is inappropriate, because it may in fact be a more reasonable approach to determining who will benefit from CC. There is no evidence in the literature to suggest why a low-risk patient would benefit from CC at all, irrespective of sex/gender. Evidence of survival benefit from revascularization has only been demonstrated among high-risk patient groups (37,38).

Our study also revealed that physicians perceive younger patients as more likely to benefit from CC than older patients. This finding was reinforced in that physicians identified chest pain among younger patients as more likely to be cardiac than such chest pain in older patients. It may also reflect the belief that younger patients benefit more from early diagnosis of CAD in terms of potential years of life lost than older patients, despite trends of actual risk (1). For this reason, physicians may be more driven to make a diagnosis among younger patients. In our study, a 75-year-old, low-risk patient was perceived to be significantly less likely to benefit from CC than a 55-year-old patient of equal risk. This contradicts the epidemiology of CAD, which demonstrates a greater probability of CAD among older patients. Interestingly, other studies have also reported that younger patients, and not necessarily higher risk patients, are more likely to be referred for invasive procedures (31,39).

When we evaluated risk, both as a main effect and as an interaction term, high-risk patients were identified appropriately and seen to benefit the most from CC. Our assessment of risk was internally valid because physicians identified increasing risk for MI as the TIMI risk was increased in the scenario. This finding was particularly evident among high-risk scenarios, in which patient factors such as sex/gender, age or expressed patient preference did not influence the physician's decision to refer. However, the same was not true among low- and moderate-risk patients. Low- and moderate-risk patients who expressed a desire for CC were more likely to receive a CC than patients who refused or expressed no opinion at all. This suggests that while high-risk patients are being appropriately referred for CC, greater standardization of catheterization referral in low- and moderate-risk patient groups is needed because CC is not a procedure without risk, and these risks may not outweigh the benefit, particularly among low-risk patients.

Limitations

To recruit physicians for our study, we used nonrandom sampling of Canadian cardiologists and internal medicine specialists, and the response rate to our invitation was low; thus, some respondent bias likely exists. At the same time, we invited specialists to participate in our study via an e-mail invitation only because the present study used a web-based instrument. In today's Internet world of increasing firewalls, spam, junk and other protective e-mail filters, we are uncertain how many physicians we actually reached; therefore, our true denominator remains unknown. However, despite a small sample size, physicians sampled in our study are representative of the actual distribution of physicians across Canada. Furthermore, the characteristics of the physicians who responded to our survey reflect the current characteristics of cardiac specialists in Canada, where most specialists are men who have been practicing for at least 10 years (40) and women represent less than one-half of their patient population. It is important to note that the responders were blinded to the intent of the study, which was to identify sex/gender differences in CC referral. Scenarios were randomly allocated to each physician, so it is unlikely that there was any internal bias. Also, the subtleties and complexities of human interaction cannot be fully captured in paper scenarios, although previous studies have shown that the response to hypothetical case scenarios parallels real-world decision making (41,42). Finally, to represent risk, we used the TIMI risk score because this is the most popular, validated ACS risk score (43-46) and this was reflected by our sample, in which almost 75% of the physicians surveyed who used a risk score reported using the TIMI risk score. Also, the use of the TIMI risk score is internally valid because physicians correctly assessed increasing risk according to the TIMI risk score (P<0.001).

CONCLUSION

Canadian specialists' decisions to refer patients for CC appear to be influenced by sex/gender, age and patient preference in clinical scenarios in which cardiac risk is held constant. Future investigations into possible age and sex/gender biases as well as a better understanding of how physicians use these factors as proxies for risk are warranted.

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APPENDIX A

Sample of a clinical vignette scenario

RM is a 75-year-old individual who presents to the ER with retrosternal chest pain radiating down both arms. RM is also experiencing dyspnea and nausea, and claims a history of heart problems but has been well controlled until this ER visit. RM took three nitrosprays to relieve the chest pain, but it did not completely resolve itself as it had in the past.

RM's medical history includes a myocardial infarction seven years ago and an angioplasty to the RCA during that hospital stay. Cardiovascular risk factors include type 2 diabetes, hypertension and half-pack/day smoking history. There is no history of hypercholesterolemia. RM also reports that a younger brother had bypass surgery at 54 years of age.

Current medications include EC ASA 325 mg o.d., metformin 500 mg b.i.d., ramipril 5 mg o.d. and nifedipine XL 60 mg o.d., with nitroglycerin spray as needed.

On examination, height is 166 cm and weight is 72 kg. Blood pressure is 110/85, and HR is 108 and regular. Chest sounds are clear. On precordial examination, heart sounds are normal with a II/VI pansystolic murmur heard loudest at the apex. JVP is mildly elevated and has mild peripheral edema.

ECG on arrival shows a 1.5 mm ST segment depression in V1 to V3. Troponin and CK are slightly elevated. CBC, electrolytes and creatinine are normal.

RM is resting quietly while you try and locate old notes from the last hospital visit.

APPENDIX B

Physician questions

1. Physician name: First, middle initial, last name.
2. Work address: Number, street, city, province, postal code, telephone number.
3. Name of practising hospital.
4. E-mail address.
5. Sex: male/female.
6. Number of years practising medicine.
7. Specialty.
8. An estimate of the percentage of female patients seen in practice.
9. An estimate of the percentage of white Caucasian patients seen in practice.
10. Presence of on-site catheterization laboratory at your hospital.
11. Do you use any risk assessment score in your decision to refer a patient for cardiac catheterization? ie, FRISC score, TIMI score, GRACE score, other _____.
12. Type of practice: Academic centre, community-based, outpatient clinic only, other _____.

APPENDIX C

Vignette questions

Scenario questions:

1. How would you characterize this patient's risk of suffering a fatal or nonfatal MI in the next 14 days?
   ❒ *Low risk* ❒ *Moderate risk* ❒ *High risk*
2. How would you characterize this patient's chest pain?
   ❒ *Noncardiac* ❒ *Possibly cardiac* ❒ *Definitely cardiac*
3. What is the likelihood that this patient would benefit from a cardiac catheterization procedure?
   ❒ *Very unlikely* ❒ *Somewhat unlikely* ❒ *Unsure*
   ❒ *Somewhat likely* ❒ *Very likely*
4. Estimate the probability that this patient has a significant CAD (or stenosis >70%).
   ❒ *Very unlikely* ❒ *Somewhat unlikely* ❒ *Unsure*
   ❒ *Somewhat likely* ❒ *Very likely*
5. If you decide to not refer this patient for catheterization, would you order any further tests?
   ❒ *Yes* ❒ *No*
   If so, which of the following?
   ❒ *Stress test* ❒ *Stress test and thallium*
   ❒ *Cardiac function assessment* ❒ *Other* _____
6. How much does the patient's preference influence your decision to refer them for catheterization?
   ❒ *Not much at all* ❒ *Not a lot* ❒ *Unsure*
   ❒ *A fair amount* ❒ *To a great extent*
7. Do you need any more information to make your decision regarding further testing?
   ❒ *Yes* ❒ *No*
   If so, what information would you require? _____
   _____.

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